restriction of free rotation about the single bond between the imino nitrogen and the isopropyl methine carbon due to the access of the (*S*,*S*)-**1** molecule. From the foregoing discussion, the involvement of the imino nitrogen of (*R*,*R*)-**2** in the association appears quite likely, and this would confirm the associated structure depicted in Figure 1 as responsible for the enantioselection noted in the present study.

In summary, we have developed a representative of a new chiral selector that employs the complementarity of twists in dual hydrogen bond association. We are currently extending the scope of enantioselection by the present selector to reveal the generality of this approach to molecular recognition.

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Oxidative Organic Electrochemistry: A Novel Intramolecular Coupling of Electron-Rich Olefins

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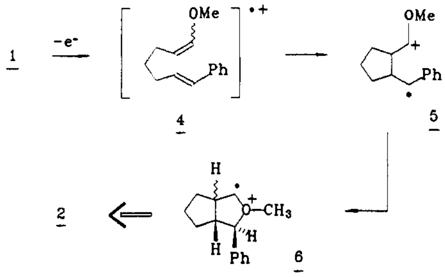
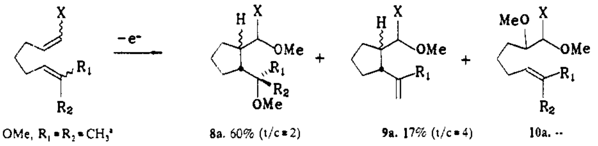
Oxidative cyclization reactions are of interest because they allow for the generation of carbon–carbon bonds and the formation of rings without a loss in the overall functionality of a molecule.[1,2] Organic electrochemistry would appear ideally suited for initiating such reactions because it can selectively oxidize electron-rich functional groups at preset potentials, under neutral conditions, and without the need for chemical reagents.[3] Unfortunately, there exist only a few examples of anodic reactions that lead to direct carbon–carbon bond formation.[4] In addition, only a handful of these reactions have been shown to be generally useful for initiating intramolecular cyclization reactions.[5,6] We report herein our initial efforts to develop the anodic coupling of electron-rich olefins for such a purpose.[7,8]

Scheme I



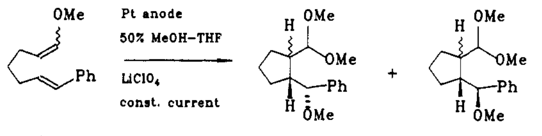
Scheme II[a]



7a. X = OMe, $R_1 = R_2 = CH_3$[a]	**8a.** 60% (t/c = 2)	**9a.** 17% (t/c = 4)	**10a.** --
7b. X = Ph, $R_1 = R_2 = CH_3$[a] (6% recovered)	**8b.** 15%	**9b.** 5%	**10b.** 25%
7c. X = OSi(i-Pr)$_3$, $R_1 = R_2 = CH_2$[b]	**8a.** 48% (X = OMe)	**9a.** 19% (X = OMe)	**10c.** --
7d. X = OSi(i-Pr)$_3$, R_1 = Ph, R_2 = H[c] (9% recovered)	**2/3.** 57% (X = OMe: 2/3 = 1.7) **8d.** 10% (X = OSi(i-Pr)$_3$, R_1 = Ph, R_2 = H)	**9d.** N.A.	**10d.** --

[a] Conditions: (a) Pt anode, MeOH, $LiClO_4$, 2,6l-lutidine, divided cell; (b) Pt anode, 50% MeOH/THF, $LiClO_4$, undivided cell; (c) Pt anode, 10% $MeOH/CH_3CN$, $LiClO_4$, undivided cell.

These studies were initiated by examining the electrochemical behavior of compound **1**. To this end, *the anodic oxidation of **1** under constant-current conditions in an undivided cell using a platinum anode and a 1 N lithium perchlorate in 50% methanol–tetrahydrofuran electrolyte solution led to 68–73% isolated yields of cyclized products.* To our surprise, the reaction afforded a moderate degree of diastereoselectivity and gave rise to a 5.3:1 mixture of isomers at the benzylic carbon (compounds **2** and **3**). The cyclization also resulted in cis and trans isomers about the five-membered ring. The cis and trans isomers having the same stereochemistry at the benzylic carbon were identified by hydrolysis of the acetals and then epimerization of the products to a single aldehyde isomer. The stereochemistry at the benzylic carbon was determined by a single-crystal X-ray analysis of the 2,4-dinitrophenylhydrazone (2,4-DNP) derivative derived from the trans major aldehyde.[9]



1 2 (a=cis) (t/c=1) (b=trans) 3 (t/c=3)

(Yield = 68−73%, Ratio of 2 to 3 = 5.3/1)

[†] Author to whom correspondence concerning the X-ray analysis should be addressed.

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(4) (a) For reviews, see refs 3b–d (especially ref 3b, Appendix 1.1, and ref 1c, Chapter 4) as well as the following: Schafer, H. J. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 911. For a couple of recent examples, see: (b) Yamamura, S.; Shizuri, Y.; Nakamura, K. *J. Chem. Soc., Chem. Commun.* **1985**, 530. (c) Yoshida, K.; Sakaguchi, K.; Isoe, S. *J. Org. Chem.* **1988**, *53*, 2525. Yoshida, J.; Sakaguchi, K.; Isoe, S. *Tetrahedron Lett.* **1986**, *27*, 6075.

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(8) In a somewhat related study, Shono has reported the anodic intramolecular coupling of enol acetates and olefins in moderate yields (18–40%). Shono, T.; Nishiguchi, I.; Kashimura, S.; Okawa, M. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 2181.

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Evidence concerning the origins of the observed diastereoselectivity was obtained by repeating the reaction using 50% MeOH-d_4/THF as solvent. In this case, anodic oxidation of **1** led to a 68% yield of cyclized products. Compounds **2** and **3** were again formed in a 5.3:1 ratio (the compounds had OCD_3 acetals). NMR analysis showed that approximately 50% of the cyclized material *still had an* OCH_3 *group at the benzylic position* and therefore had to be derived from intramolecular transfer of the methoxy group originally at C_1 of the starting material. This material was predominately (greater that 10:1) the cis and trans major products, **2**. The remainder of the material had an OCD_3 group at the benzylic position and was formed in a ca. 2:1 ratio of cyclized products **2** and **3**. These products are assumed to arise from solvent trapping of an incipient benzylic carbocation.

The methanol-d_4 experiment suggests that the bulk of the diastereoselectivity was derived from an intramolecular transfer of the C_1 methoxy group and that at one point half of the material must pass through a bicyclic intermediate like **6** (Scheme I). The stereochemistry of the major products can be explained by suggesting that the phenyl ring occupies the sterically least hindered position in this bicyclic intermediate. Although the possibility of a trans-fused bicyclic intermediate is troublesome, OCH_3 ether products having both cis and trans stereochemistry about the five-membered ring are formed (1:1 ratio), and the lack of *any* deuterium incorporation at the bridgehead positions rules out the possibility of the trans product resulting from epimerization of a cis product. A mechanism wherein either **4** or **5** is trapped by solvent to form a mixed OCH_3/OCD_3 acetal prior to migration seems unlikely in view of the difference in diastereomer ratios obtained for the OCH_3 and OCD_3 benzyl ether products.[10]

Having determined that the anodic oxidation of **1** could cleanly lead to intramolecular coupling products, we turned our attention to examining whether the enol ether, the styrene, or both groups were necessary for effective cyclization.[11] In order to address this question, we synthesized cyclization substrates **7a** and **7b**. Preparative electrolysis of **7a** in methanol led to the formation of a 77% isolated yield of cyclized products (Scheme II). These products were obtained in a ca. 3.5:1 ratio of compounds **8a** and **9a**. No uncyclized material was obtained. On the other hand, anodic oxidation of **7b** in methanol led to a complex mixture of products. From the 300-MHz ^1H NMR spectrum of the crude reaction mixture it was clear that the majority of the material was not cyclized. From the mixture, four major compounds were obtained along with 6% of the recovered starting material. Two of the compounds were uncyclized and were isolated in 25% yield. A 20% yield of cyclized materials was obtained. It is clear from these results that anodic oxidation of the enol ether is much more effective at initiating the intramolecular coupling reactions than is oxidation of the styrene moiety.

Finally, the reactions were studied in order to see if silyl enol ethers would be compatible with the electrochemical oxidation conditions. To this end, silyl enol ether substrates **7c** and **7d** were studied. Electrolysis of **7c** led to the formation of a 67% isolated yield of dimethoxy acetal products **8a** and **9a**. These products were obtained in a 2.6:1 ratio, respectively. Anodic oxidation of **7d** led to the formation of a 67% isolated yield of cyclized products **2**, **3**, and **8d**, along with 9% of the recovered starting material. The products were obtained in a combined 1.8:1 mixture of isomers at the benzylic position. In neither case was any uncyclized material isolated. The use of silyl enol ether initiators should greatly expand the synthetic utility of the reactions because of the ease of their synthesis.

In summary, we have found that the intramolecular anodic coupling of enol ethers and olefinic nucleophiles can lead to high yields of cyclized products.[12] *These examples represent a new class of potentially useful anodic carbon–carbon bond forming reactions.* Studies aimed at further elucidating the factors that govern product formation and diastereoselectivity as well as determining the overall synthetic utility of these reactions are currently underway. The results of these studies will be reported in due course.

Acknowledgment. This work was supported by the donors of the Petroleum Research Fund, administered by the American Chemical Society, and by the Biomedical Research Support Program, Division of Research Resources, National Institutes of Health. We also gratefully acknowledge the Washington University High Resolution NMR Facility, partially supported by NIH 1S10R02004, the Washington University Mass Spectrometry Resource Center, partially supported by NIHRR00954, and Washington University's X-Ray Crystallography Facility, funded by the National Science Foundation's Chemical Instrumentation Program (Grant CHE-8811456), for their assistance.

Supplementary Material Available: A sample experimental procedure for the electrochemical cyclization reaction along with characterization data for compounds **1–3** and **7–10** and a structure determination summary for the 2,4-DNP derivative derived from **2** (18 pages); a list of observed and calculated structure factors for the 2,4-DNP derivative derived from **2** (25 pages). Ordering information is given on any current masthead page.

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(9) Crystallographic data for $C_{20}H_{22}N_4O_5$: mol wt 398.4; triclinic, space group $P\bar{1}$ (No. 2); $a = 7.236$ (2) Å, $b = 17.036$ (6) Å, $c = 17.134$ (6) Å, $\alpha = 86.03$ (3)°, $\beta = 82.64$ (3)°, $\gamma = 68.79$ (2)°, $V = 1953$ (1) Å^3, $\rho = 1.355$ g/cm^3 for $Z = 4$ at 22 °C, $\mu = 0.93$ cm^{-1} (Mo Kα, $\lambda = 0.71073$ Å). A total of 7464 reflections were collected using SIEMENS R3m/V automated diffractometer. The structure was solved by direct methods. Full-matrix least-squares refinement using 3610 observed $[F > 6J(F)]$ reflections out of 6868 unique reflections gave a final $R = 0.0467$ and $R_w = 0.0315$.

(10) At this point no evidence has been obtained to indicate when the second electron is removed. The trapping of electrochemically generated radical cations with methoxy radicals is well precedented: Dolson, M. G.; Swenton, J. S. *J. Am. Chem. Soc.* **1981**, *103*, 2361. Nilsson, A.; Palmquist, U.; Pettersson, T.; Ronlan, A. *J. Chem. Soc., Perkin Trans. 1* **1978**, 7, 708.

(11) Interestingly, both groups have similar oxidation potentials. For example, cyclic voltammetry of both **4a** and **4b** gives rise to an initial oxidation wave at +1.4 V vs a Ag/AgCl reference electrode (Pt anode/1 N $LiClO_4$ in CH_3CN).

(12) Recently, a chemical variant to these reactions has been reported for phenyl-substituted silyl enol ethers. Snider, B. B.; Kwon, T. *Abstracts of Papers*, 199th National Meeting of the American Chemical Society, Boston, MA; American Chemical Society: Washington, DC 1990; ORGN 322.

Models of the Cytochromes *b*. 7. Novel Features in the Proton Nuclear Magnetic Resonance Spectra of Mono-Ortho-Substituted Dialkylamido Tetraphenylporphinatoiron(III) Complexes

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For some time it has been proposed that the effects of hindered axial ligand rotation and fixed axial ligand orientation may be significant for the regulation of midpoint potentials[1] and for the explanation of unusual shifts of certain resonances in the proton NMR spectra of heme proteins.[2-4] These suggestions have stimulated a number of investigations to determine the role of these effects in heme proteins and model heme compounds.[5-10]

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